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Short Communication

A mild and efficient method for the preparation of substituted Benzimidazole derivatives from o-phenylene diamine and various aromatic aldehydes catalysed by cation exchange resins

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Abstract

The present method provides a green route for the synthesis of substituted benzimidazoles .The reactions are carried out at moderate temperature and in the presence of cation exchange resins like Amberlyst, Tulsion, Indion. The conversions are quantitative and the products thus obtained are characterised by UV, IR and PMR spectroscopic methods.

Keywords: Benzimidazoles, Cation exchange resins, Green route.

Introduction

Benzimidazoles are important class of fused heterocyclic compounds in which benzene ring is fused with 1,3-azoles[1-4]. Benzimidazoles are well known for their medicinal properties and are used extensively in the pharmaceutical industries[5]. The presence of heterocyclic ring is a key feature responsible for the various biological activities. These molecules are primarily used as anticancer drugs by the virtue of benzimidazole moiety[6]. Omeprazole is the derivative of benzimidazole which used as gastric proton-pump inhibitor and antiulcer agent. The other therapeutic uses are also known in the literature.

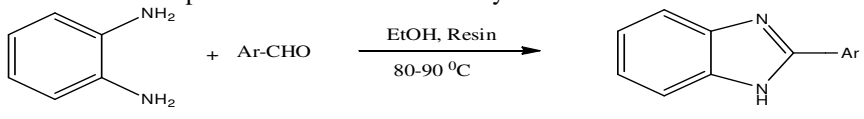
Most of the benzimidazole are available through ring synthesis way from ortho heteroatom substituted aromatic compounds. The structural feature can be achieved through condensation of 1, 2-aromatic diamine and an aromatic aldehydes[7] as one of the preparative method. This method has limitations as it yields mixture of products. The reaction of o-phenylene diamine with any one of the reagents from aromatic acids, nitriles, orthoesters, imidates is widely employed because of the better yield of the desired product[8]. Copper acetate, lead tetra-acetate and Rh, Ru and Pd catalysts are also known to affect this condensation reaction[9].

When aliphatic or aromatic aldehyde reacts with o-phenylene diamine in presence of nitrobenzene in presence of silica to form derivatives of 2-substituted imidazole[10]. Most of these reactions furnish low yield of benzimidazoles or the reaction conditions are drastic and the single product formation becomes remote. The transition metals are better catalysts but due to their high cost they are seldom used in the chemical laboratories.

Materials and methods

The reagents and chemicals were commercially available from Sigma-Aldrich and when needed, were purified using normal purification techniques.

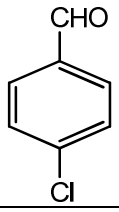
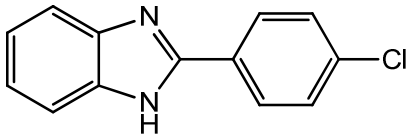
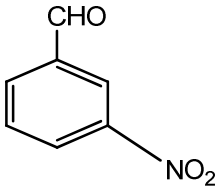
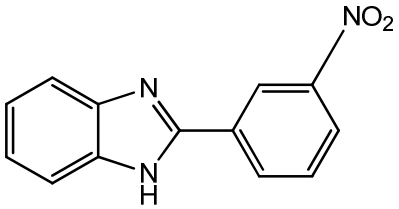
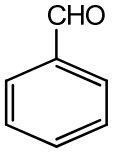
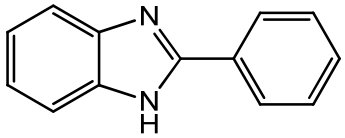
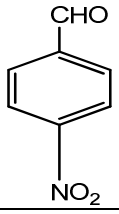
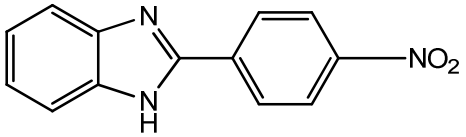
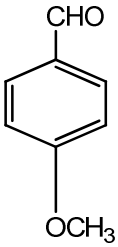
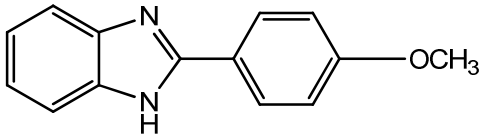
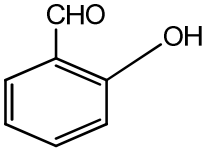
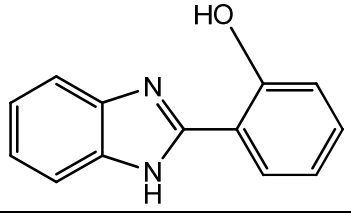
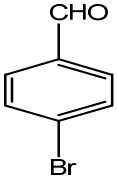
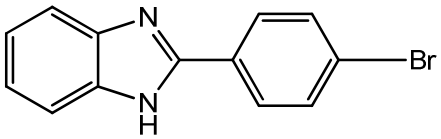
Synthesis of substituted benzimidazole derivatives: The present procedure involes condensation of o-phenylene diamine and aromatic aldehydes in ethanol solvent in Scheme-1. 1 gm (9 mmoles) of o-phenylene diamine is dissolved in 15 ml of ethanol. To this 1.29 gm (9 mmoles) of p-chloro benzaldehyde is added as an ethanolic solution. 100 mg of cation exchange resin is used as a catalyst for this condensation reaction. The reaction mixture is heated on water bath at 80^0C for 3-4 hours. The progress of the reaction is monitored by TLC. Once the reaction is complete, the catalyst is removed by filtration of reaction mixture through Whatmann filter paper. The evaporation of ethanol furnished crude benzimidazole. This is further purified by crystallisation form ethanol or column chromatography. The structure was determined by spectral analysis.



o-phenylene diamine Benzimidazole derivatives (1-7)

Scheme-1: General Procedure for Synthesis of substituted Benzimidazole derivatives.

Table-1: Synthesis and Characterisation of Benzimidazole derivatives.

Compound No.	Aromatic aldehyde	Final Product	TLC Solvent
1			Ethyl acetate: Pet ether 1 : 4
2			Ethyl acetate: Pet ether 1 : 4
3			Ethyl acetate: Pet ether 1 : 4
4			Ethyl acetate: Pet ether 1 : 4
5			Ethyl acetate: Pet ether 1 : 4
6			Ethyl acetate: Pet ether 1 : 4
7			Ethyl acetate: Pet ether 1 : 4

Results and discussion

The results of the condensation reactions are summarised in Table-2.

The other cation exchange resins like Tulsion and Indion are also used as a catalyst in the below reactions.

Aldehydes possessing electron withdrawing groups react faster. These findings are in accordance to the electron availability at carbonyl center of an aldehyde.The electron acceptors promote nucleophilic attack and thereby the formation of benzimidazole.

The electron donors on the other hand retard the reaction rate by supplying electrons to the rings, which effectively reduce the electrophilic character of carbonyl group.

The Spectroscopic data of the benzimidazole derivative of compound 1 is as follows:

Compound-1: IR (cm^{-1}) (KBr) 3734, 1683,1540, 668 and 597. ^1H NMR (500 MHz, DMSO-D_6) δ - 8.15 (d, 2H), 7.6-7.9 (m, 2H) and 7.2 -7.6 (m, 4H)

Table-2:

Sr. No.	Aromatic Diamine	Aromatic Aldehyde	Catalyst	Reaction Time	% Yield of the Product	M.P. / ^{0} C
1	o-Phenylene Diamine	p-chloro benzaldehyde	Amberlyst	4 hrs	85 %	290
2	o-Phenylene Diamine	m-nitro benzaldehyde	Amberlyst	3 hrs	88 %	300
3	o-Phenylene Diamine	Benzaldehyde	Amberlyst	4 hrs	78 %	282
4	o-Phenylene Diamine	p-nitro benzaldehyde	Amberlyst	3 hrs	86 %	324
5	o-Phenylene Diamine	p-Anisaldehyde	Amberlyst	4 hrs	80 %	216
6	o-Phenylene Diamine	Salicylaldehyde	Amberlyst	4 hrs	80 %	239
7	o-Phenylene Diamine	p-bromo benzaldehyde	Amberlyst	3 hrs	83 %	300

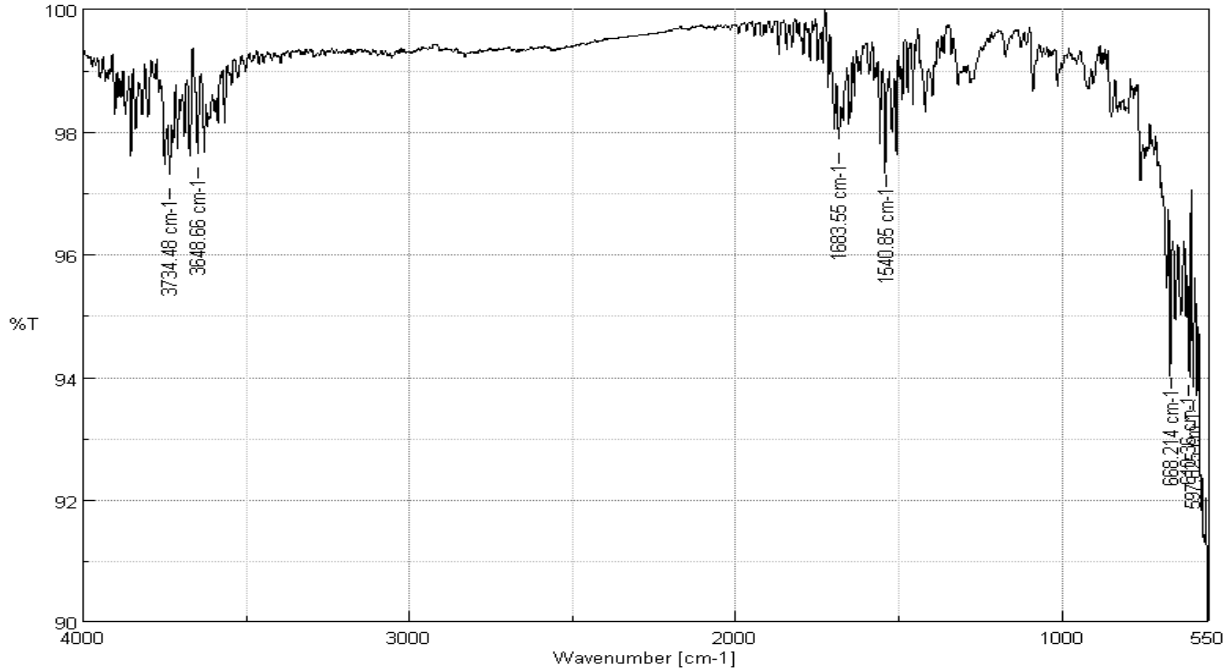


Figure-1: IR spectrum of Compound 1

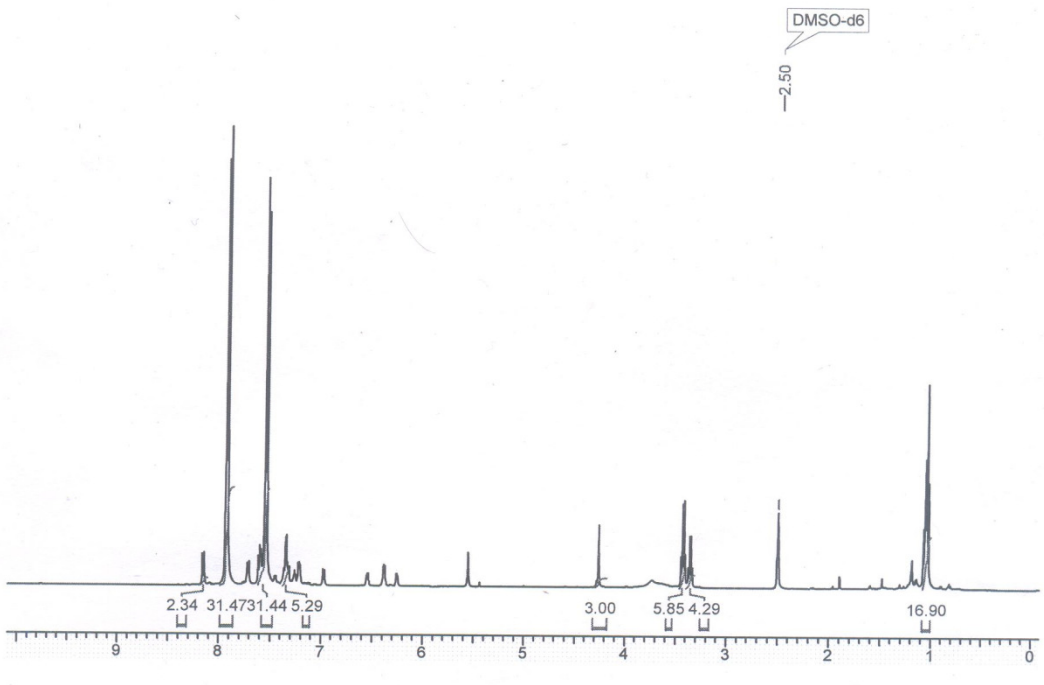


Figure-2: NMR spectrum of Compound 1.

Conclusion

The resin catalysed condensation provides a mild and clean method for the synthesis of benzimidazole derivatives from the o-phenylene diamine and aromatic aldehydes. These reactions are very easily carried out in the chemical laboratory and the yields are very good. This method is ecofriendly and follows green chemistry norms.

Acknowledgements

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